REMARKS/ARGUMENTS

ELECTION OF THE CLAIMS

A. Between Groups I and II

In response to the requirement to elect the claims of Group I or II, Applicants hereby elect the claims of Group I, i.e., claims 1-14, 19, and 20 drawn to a compound 8 to 50 nucleobases in length targeted to a nucleic acid molecule encoding ABC transporter MHC 1, wherein said compound specifically hybridizes with said nucleic acid molecule encoding ABC transporter MHC 1 and inhibits the expression of ABC transporter MHC 1, without traverse.

Applicants reserve the right to re-present claims 15-18 when the composition claims 1-15 and 19-20 are found allowable.

B. Between Sequences of Claim 3

In response to the requirement to elect one (1) antisense oligonucleotide of claim 3, Applicants respectfully make the following provisional election and traverse this portion of the restriction requirement.

(1) PROVISIONAL ELECTION OF CLAIM 3

In response to the outstanding requirement in which Applicants are required to elect an antisense compound from claim 3, Applicants provisionally elect, with traverse, the antisense oligonucleotide of SEQ ID NO: 37.

(2) REMARKS AND TRAVERSAL OF RESTRICTION REQUIREMENT TO ELECT ONE SEQUENCE OF CLAIM 3

The claims pending after amendment are claims 1-20. Claims 15-18 stand withdrawn as being drawn to nonelected subject matter. Applicants reserve the right to represent claims 15-18 when the composition claims 1-15 and 19-20 are found allowable. Applicants affirm the correctness of the inventive entity in view of the election of claims.

As noted above, Applicants have provisionally elected with traverse SEQ ID NO: 37 of claim 3.

However, Applicants traverse the restriction requirement for three primary reasons. The logical result of such a narrow restriction requirement effectively deprives Applicants of the right to obtain patent protection on a reasonable scope of the invention. Additionally, the restriction requirement should more properly be a species restriction. Thirdly, the Restriction to a single sequence contravenes the policies of the Commissioner.

(a) Such a narrow restriction requirement effectively deprives Applicants of the right to obtain patent protection on a reasonable scope of the invention.

Applicants are well aware, and respectfully acknowledge, that the workloads of the USPTO examiners are such that every search of a claimed invention must have an element of burdensomeness. Applicants have great respect for the examiners and the level of work they handle. However, the reasonableness of the amount of searching that

must be done by the examiner on a single application should, in all fairness, be balanced by the "unreasonableness" of the burden placed upon the Applicant/inventor by any arbitrary limitation of the scope of that search. Applicants submit that the limitation of the claims of this application to a single sequence by the present restriction requirement is unreasonable on its face.

In the present case, the logical conclusion of such a restriction requirement would result in these Applicants filing at least 79 different applications to cover only the target sequences shown in Table 1, and all of that expense and effort for a single target gene, ABC transporter MHC 1. No Applicant/inventor is likely to be able to afford the effort and expense of filing such an onerous number of patent applications in order to cover the full scope of his invention. This is particularly true where the invention involves multiple species that can be encompassed by a single generic claim.

The logical result of the application of this type of restriction requirement is to ***discourage*** Applicants from filing patent applications on valuable inventions. Such discouragement is not, or at least should not be, the purpose or the practice of the United States Patent and Trademark Office.

(b) The Restriction Requirement of Claim 3 Should More Properly Be a Species Election

The antisense compounds of the present invention each target and modulate the expression of the same ABC transporter MHC 1 of SEQ ID NO: 3. Applicants freely admit that this gene is within the prior art. The present invention involves compounds that specifically hybridize within certain portions of the ABC transporter MHC 1 gene and inhibit expression of the gene. The target regions illustrated in Table 1 are representative target regions of the ABC transporter MHC 1 gene, spanning nucleotides 1-2247 of SEQ ID NO: 3, that provide good targets of antisense inhibition of ABC transporter MHC 1 expression.

Another common trait of these target sequences is that they mediate greater than 61% inhibition of the MHC 1 gene in a human cell that expresses ABC transporter MHC 1, when the cell is contacted by antisense sequences. Inhibition may be measured in a variety of suitable assays described in the specification for that purpose. For example, a qualitative RT-PCR assay was employed to provide the inhibition data presented in Table 1 of the specification. This latter inhibition percentage requirement has been added to claim 1 to clarify this invention.

Each target sequence of Table 1, while an independent and distinct sequence in its own right, is a ***SPECIES*** of the ***GENUS*** defined in amended claim 1. That genus is composed of sequences of 8 to 30 consecutive nucleobases in length, found within nucleotides 1-2247 of SEQ ID NO: 3, and that when bound to a compound that

specifically hybridizes to that sequences, mediates greater than 61% inhibition of the MHC 1 gene in a human cell, as measured in a suitable assay, e.g., a qualitative RT-PCR assay. Clearly, each such target sequence of Table 1 is a species of a well-defined and readily identified genus.

The procedure for handling applications that include generic claims is set forth in 37 CFR § 1.146. This rule provides that:

> "[I]n the first action on an application containing a generic claim to a generic invention (genus) and claims to more than one patentably distinct species embraced thereby, the examiner may require the applicant in the reply to that action to elect a species of his or her invention to which his or her claim will he restricted ***if no claim to the genus is found to be allowable.***" (emphasis added)
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> As stated in MPEP § 809.02(a):
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> "...upon allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR § 1.141."

Where generic claims are present an applicant ***may*** be required to elect a species for initial examination, but the generic claims are still subject to examination to determine whether such generic claims are allowable.

MPEP § 806.04(b) states that species may be related inventions. Specifically, this section of the MPEP directs that:

> "[w]here inventions as disclosed and claimed are both (A) species under a claimed genus and (B) related, then the question of restriction must be determined by both the practice applicable to

> election of species and the practice applicable to other types of restriction such as those covered in MPEP § 806.05-§806.05(i). If restriction is improper under either practice, it should not be required."

The species set forth in claim 3 (particular oligonucleotide sequences) fall within the genus of claim 1 (compounds targeted to a nucleic acid encoding ABC transporter MHC 1) and the subgenus of claim 2 (antisense oligonucleotide compounds targeted to a nucleic acid encoding ABC transporter MHC 1). The species are also related; each species is a compound which both targets and inhibits the expression of ABC transporter MHC 1 and may even overlap. Therefore, as described above, "the question of restriction ***must*** be determined by both the practice applicable to election of species and the practice applicable to other types of restriction such as those covered in MPEP § 806.05-§806.05(i)". In the present case, restriction must be determined by the practice applicable to election of species. The practice applicable to the types of restriction such as those covered in MPEP § 806.05-806.05(i) is clearly not relevant to the present invention.

As MPEP § 806.04(b) states that species that are related inventions must be determined by both the practice applicable to election of species and the practice applicable to other types of restriction such as those covered in MPEP §806.05-806.05(i). The rules detailed by MPEP §806.05-806.05(i) are not relevant to the present invention.

As such, Applicants respectfully request that the examiner reconsider this restriction requirement and convert it into a species restriction. In this way, the patentability of the generic claim may be preserved in the event that a search of the species does not prove fruitful. These claims clearly appear much more suited to a species election than a restriction.

(c) The Restriction to a Single Sequence Contravenes the Policies of the Commissioner.

According to MPEP 803.04 and 2434, up to 10 *independent and distinct* nucleotide sequences can be examined in a single application. The apparently arbitrary decision that only one sequence will be searched in this application is a contradiction of this USPTO policy. The Examiner provides as the rationale for the restriction that "...each antisense sequence claimed is structurally and functionally *independent and distinct*..." for the reasons set out in page 3, line 12 through page 4, line 7 of the Action.

However, as noted in the MPEP sections cited above, the independent and distinct nature of the sequences is **not** a reasonable basis on which to determine that a single sequence should be examined, since the Commissioner in his policy noted that multiple such sequences could be searched in a single application. In fact, the examiner's rationale contradicts the intent and very wording of the Commissioner's decision embodied in the MPEP.

With respect, the examination of more than a single sequence in this application is believed not to be

an undue burden on the USPTO. The examiner is correct that each target region has a unique sequence. That very "unique sequence" however, should not of itself mean that any search involving multiple such unique sequences is automatically "undue". Despite the "complex nature" of the subject matter, a computer search for sequence comparisons, e.g., a BLAST search, which is properly directed to the target sequence (e.g., SEQ ID NO: 3 or fragments thereof) and for which certain percent homology or mismatch parameters can be requested, is a method to search sequences which is not unduly time-consuming. The BLAST algorithm, when run using only the default settings, will locate identical, complementary and inverted nucleic acids. The output will also designate the strandedness, hence the relationship between the query sequence (in this case SEQ ID NO: 3 or a fragment) and the "hits" it locates. Furthermore, minor changes to the search parameters in combination with database selections allows an even faster search for sequences covered by the scope of the claims. For example, if the claim is limited to a taxonomic species, like humans, that filter can be selected before the search is executed, greatly diminishing the burden on the Examiner to search through multiple off-species results.

Clearly, sense versions of portions of the MHC 1 are undoubtedly in the prior art, but may be excluded as they are not the claimed subject matter. A proper BLAST search would eliminate any hits for sense sequences, and could be conducted very quickly. Applicants respectfully submit that conducting multiple such BLAST searches is not

necessary for the foregoing reasons. Even if multiple searches were considered necessary, such searches would not require undue or unreasonable additional time.

Further, considering the requirement for specific hybridization of an antisense sequence to a "target" fragment or region of SEQ ID NO: 3, the fact that the examiner must search different 8-nucleotide to 30-nucleotide "places" in SEQ ID NO: 3 also does not appear to be evidence of an unreasonable search requirement, as all of the "places" are found in a single sequence, SEQ ID NO: 3.

Applicants respectfully request that in view of the above-noted elections and the above remarks, that the examiner reconsider and withdraw this restriction requirement as applied to claim 3.

The Director is hereby authorized to charge any additional fees required with the filing of this paper or credit any overpayment in any fees to our deposit account number 08-3040.

Respectfully submitted,

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